EE145B: Compartmental Modelling

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Basic Definitions

A Compartmental system is composed of a finite number of macroscopic *compartments* or *pools*.

Compartments contain and exchange material. They are homogeneous and well-mixed.
They do not, in general, correspond to physical volumes or spaces.

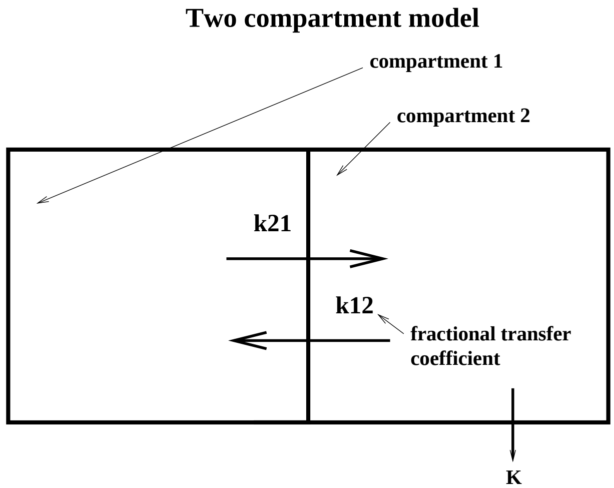
Closed systems have no input or output to environment.

Open systems may have input to or output from any compartment.

Fractional transfer coefficients tell us what fraction of a compartment is exchanged per unit time.

Linear compartmental analysis involves models defined in terms of linear, constant coefficient differential equations.

A simple linear two compartment model



This system consists of two homogeneous, well-stirred compartments.

Compartment 1 contains a material at concentration x_1 kg/m^3. The size of this compartment is $q_1 = x_1 V_1$ kg.

Compartment 2 contains the same material at concentration x_2 kg/m^3. The size of this compartment is $q_2 = x_2 V_2$ kg.

A membrane of cross-sectional area A having diffusion permeability constants k_{21} and k_{12} m/s for rightward and leftward exchanges, respectively, separates the compartments.

Loss from compartment 2 to the environment occurs at rate K m^3/s.

We might model the perfusion of a radioactive tracer in the bloodstream (compartment 1) into tissue (compartment 2) using this system.

A linear system model is applicable only if we assume that the rate of transfer from a compartment is proportional to the concentration in that compartment.

Two compartment model description

This system is characterised by the simultaneous first-order differential equations:

$$\begin{aligned}
\frac{dq_1}{dt} &= -k_{21}Ax_1 + k_{12}Ax_2 && (1)\\
\frac{dq_2}{dt} &= k_{21}Ax_1 - k_{12}Ax_2 - Kx_2. && (2)
\end{aligned}$$

Using the relations:

$$\begin{aligned}
f_{12} &= k_{12}A/V_2 \text{ s}^-1 && (3)\\
f_{21} &= k_{21}A/V_1 \text{ s}^-1 && (4)\\
f_{02} &= K/V_2 \text{ s}^-1, && (5)
\end{aligned}$$

we obtain the fractional transfer coefficient representation:

$$\begin{aligned}
\frac{dq_1}{dt} &= -f_{21}q_1 + f_{12}q_2 && (6)\\
\frac{dq_2}{dt} &= f_{21}q_1 - f_{12}q_2 - f_{02}q_2. && (7)
\end{aligned}$$

These equations may be solved (possibly using the unilateral Laplace transform) to yield:

$$\begin{aligned}
q_1 &= c_1\mathrm{e}^{-m_1 t} + c_2\mathrm{e}^{-m_2 t} && (8)\\
q_2 &= c_1\left[\frac{f_{21}-m_1}{f_{12}}\right]\mathrm{e}^{-m_1 t} + c_2\left[\frac{f_{21}-m_2}{f_{12}}\right]\mathrm{e}^{-m_2 t} && (9)
\end{aligned}$$

where

$$\begin{aligned}
m_1 &= \frac{f_{12}+f_{21}+f_{02}}{2} + \frac{1}{2}\sqrt{(f_{12}+f_{21}+f_{02})^2 - f_{21}f_{02}} && (10)\\
m_2 &= \frac{f_{12}+f_{21}+f_{02}}{2} - \frac{1}{2}\sqrt{(f_{12}+f_{21}+f_{02})^2 - f_{21}f_{02}}. && (11)
\end{aligned}$$

The c_i are determined by the initial conditions of the system.

Simulation

- We may simulate *this particular* system using the closed-form expressions obtained through solution of the differential equation.

- In general, a compartmental system may have many inputs and outputs. Also, input functions are often difficult to express analytically.

- It is thus desirable to seek a method which allows simulation of these more complicated systems.

- We exploit Matlab's ability to simulate arbitrary state-space models, to perform such simulations.

A state-space model describes the time trajectories (first derivatives) of internal states of a system in terms of all other system state variables, and system inputs. The internal state-space model is described by a system of first-order differential equations:

$$\begin{aligned}
\dot{x}_1 &= a_{11}x_1 + a_{12}x_2 + \ldots + a_{1n}x_n + b_{11}u_1 + \ldots + b_{1p}u_p \\
\dot{x}_2 &= a_{21}x_1 + a_{22}x_2 + \ldots + a_{2n}x_n + b_{21}u_1 + \ldots + b_{2p}u_p \\
&\vdots \\
\dot{x}_m &= a_{m1}x_1 + a_{m2}x_2 + \ldots + a_{mn}x_n + b_{m1}u_1 + \ldots + b_{mp}u_p
\end{aligned}$$

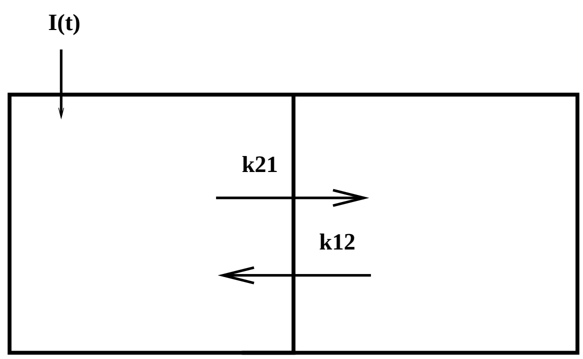
where the x_i are the system state variables and the u_i are the system inputs.

We may restate the above in matrix form as:

$$\dot{\mathbf{X}} = \mathbf{AX} + \mathbf{BU}. \tag{12}$$

Simulation continued

In compartmental analysis, a state variable might be assigned to the mass or concentration in each compartment. Thus, for the compartmental model depicted as:



whose dynamics are embodied by the DE's:

$$\frac{dq_1}{dt} = -f_{21}q_1 + f_{12}q_2 + I(t) \tag{13}$$

$$\frac{dq_2}{dt} = f_{21}q_1 - f_{12}q_2 \tag{14}$$

we find

$$A = \begin{bmatrix} -f_{21} & f_{12} \\ f_{21} & -f_{12} \end{bmatrix} \qquad B = \begin{bmatrix} 1 \\ 0 \end{bmatrix} \tag{15}$$

The general state-space model also allows us the specify how the internal states x_i of the system are measured. Measurements are allowed to depend both on the state variables and on the system inputs:

$$\begin{aligned}
y_1 &= c_{11}x_1 + c_{12}x_2 + \ldots + c_{1n}x_n + d_{11}u_1 + d_{12}u_2 + \ldots + d_{1p}u_p \\
y_2 &= c_{21}x_1 + c_{22}x_2 + \ldots + c_{2n}x_n + d_{21}u_1 + d_{22}u_2 + \ldots + d_{2p}u_p \\
&\vdots \\
y_k &= c_{k1}x_1 + c_{k2}x_2 + \ldots + c_{kn}x_n + d_{k1}u_1 + d_{k2}u_2 + \ldots + d_{kp}u_p
\end{aligned}$$

where the y_i are the system outputs measured.

Simulation continued

The corresponding matrix formulation, is:

$$\mathbf{Y} = \mathbf{CX} + \mathbf{DU}. \tag{16}$$

For the model under consideration, since we wish to consider both state variables as system output, we have the matrices:

$$C = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix} \qquad D = \begin{bmatrix} 0 \\ 0 \end{bmatrix}. \tag{17}$$

Let's see how we can use the Matlab function *lsim.m* to simulate this state-space model. The function *simtwocomp.m* illustrates this:

```
function [Y,T] = simtwocomp(f12, f21, U1, U2, t, X0)

% simulates a two compartment model given:
% f12, f21: fractional rate constants in units M/M / T
% U1, U2: input function waveforms over abscissa t for
%         compartments 1 (U1) and 2 (U2). May be empty ([]).


% prepare input function matrix U

G = zeros(2);

numinputs = 2;
U = zeros(length(t), numinputs);

if ~isempty(U1)
  U(:,1) = U1(:);
  G(1,1) = 1;
end;
```

Matlab simulation continued

```
if ~isempty(U2)
  U(:,2) = U2(:);
  G(2,2) = 1;
end;

% construct state space model matrices

A = [-f21 f12
      f21 -f12];

B = G;

C = [1 0
     0 1];

D = [0 0
     0 0];

% simulate linear system

[Y,T] = lsim(A,B,C,D,U,t,X0);
```

The use of this function is demonstrated by the script *runtwocomp.m*:

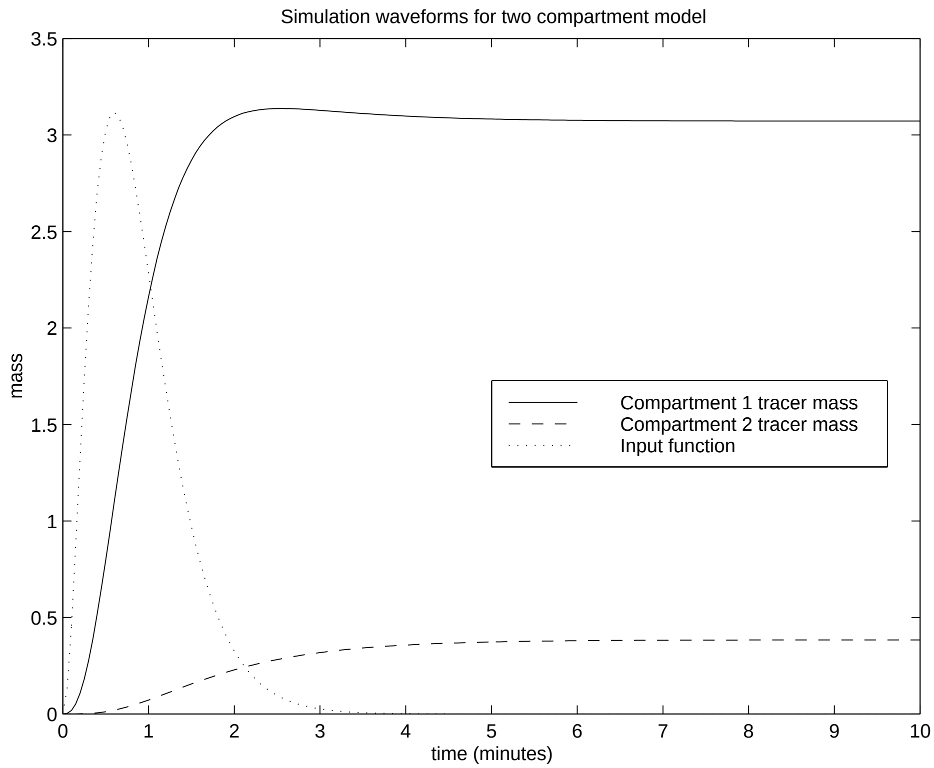
```
% script to invoke simulation of two compartment model

% set parameters

f21 = .8; % ml/ml per minute
f12 = .1; % ml/ml per minute
```

Matlab simulation continued

```
ts = .05; % sampling rate
t = 0:ts:10; % minutes

U1 = 64 * t.^2 .* exp(-t/.3); % input function for compartment 1
U2 = []; % input function for compartment 2
X0 = [.0
      .0]; % initial conditions

[Y,X] = simtwocomp(f12, f21, U1, U2, t, X0);

out1= Y(:,1);
out2= Y(:,2);

figure(1)
plot(t,out1, t, out2, '--', t, U1, ':');
legend('Compartment 1 tracer mass', 'Compartment 2 tracer mass', ...
       'Input function', 0);
title('Simulation waveforms for two compartment model');
xlabel('time (minutes)');
ylabel('mass');
```

Simulation results

Now, let's have a look what we get out of the system under these conditions:



We note that this is the response to an input function of the form

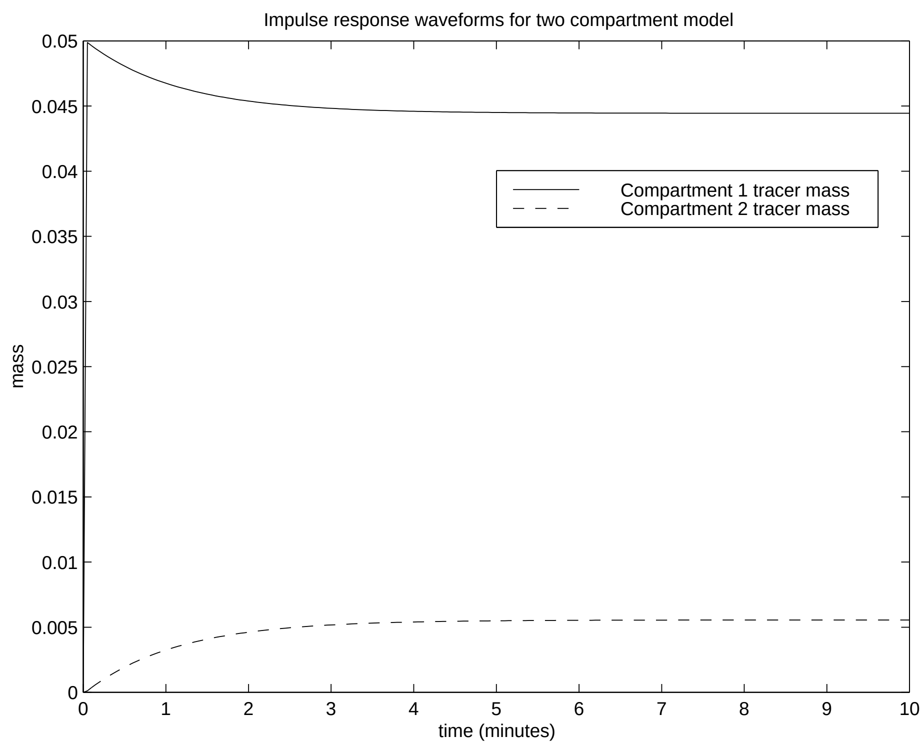
$$I(t) = C\, t^2\, e^{-\frac{t}{\tau}}, \tag{18}$$

which is an ideal approximation of a typical blood input function. We may find the system impulse response by making the alternative assignment:

```
U1 = zeros(size(t));
U1(1) = 1;
```

Simulation results

Simulation then yields:



We may also allow for the possibility of residual amounts of tracer material present in the compartments at the start of measurement:

```
X0 = [0.1
      0.3];
```

Simulation results

We observe how the presence of non-zero initial conditions complicates the forms of the responses obtained: